

PALM INTRANET

Day : Tuesday
 Date: 2/26/2002
 Time: 11:07:26

Inventor Name Search Result

Your Search was:

Last Name = BRAIS

First Name = BERNARD

Application#	Patent#	Status	Date Filed	Title	Inventor Name
<u>09590211</u>	Not Issued	071	06/08/2000	SHORT GCG EXPANSIONS IN THE PAB II GENE FOR OCULO-PHARYNEAL MUSCULAR DYSTROPHY AND DIAGNOSTIC THEREOF	BRAIS, BERNARD
<u>60152941</u>	Not Issued	159	09/09/1999	DIAGNOSIS, PROGNOSIS AND TREATMENT OF REPEAT-ASSOCIATED DISEASES AND INTRANUCLEAR INCLUSIONS-ASSOCIATED DISEASESE	BRAIS , BERNARD

Inventor Search Completed: Search Completed: No Records to Display.

Search Another:

Last Name

First Name

Inventor

(To go back use Back button on your browser toolbar.)

Back to [PALM](#) | [ASSIGNMENT](#) | [OASIS](#) | Home page

PALM INTRANET

Day : Tuesday
 Date: 2/26/2002
 Time: 11:05:36

Inventor Name Search Result

Your Search was:

Last Name = ROULEAU

First Name = GUY

Application#	Patent#	Status	Date Filed	Title	Inventor Name
<u>09508821</u>	Not Issued	041	05/26/2000	POLYMORPHIC CAG REPEAT-CONTAINING GENE AND USES THEREOF	ROULEAU, GUY
<u>09509312</u>	Not Issued	041	06/09/2000	ALLELIC VARIANTS OF THE PHOSPHOLIPASE C-YAMMA1 GENE ASSOCIATED WITH BIPOLAR DISORDER	ROULEAU, GUY
<u>09590211</u>	Not Issued	071	06/08/2000	SHORT GCG EXPANSIONS IN THE PAB II GENE FOR OCULO-PHARYNEAL MUSCULAR DYSTROPHY AND DIAGNOSTIC THEREOF	ROULEAU, GUY
<u>09718355</u>	Not Issued	019	11/24/2000	LOCI FOR IDIOPATHIC GENERALIZED EPILEPSY, MUTATIONS THEREOF AND METHOD USING SAME TO ASSESS, DIAGNOSE, PROGNOSIS OR TREAT EPILEPSY	ROULEAU, GUY
<u>09830891</u>	Not Issued	040	08/06/2001	POLYGLUTAMINE-CONTAINING PROTEINS IN NEUROPSYCHIATRIC DISORDERS	ROULEAU, GUY
<u>60152941</u>	Not Issued	159	09/09/1999	DIAGNOSIS, PROGNOSIS AND TREATMENT OF REPEAT-ASSOCIATED DISEASES AND INTRANUCLEAR INCLUSIONS-ASSOCIATED DISEASES	ROULEAU , GUY A.
<u>60167623</u>	Not Issued	159	11/26/1999	LOCI FOR IDIOPATHIC GENERALIZED EPILEPSY, MAPPING TO CHROMOSOME 2, MUTATIONS THEREOF AND METHOD USING SAME TO ASSESS, DIAGNOSE, PROGNOSIS OR TREAT EPILEPSY	ROULEAU , GUY A.

<u>60287035</u>	Not Issued	020	04/30/2001	LCI FOR IDIOPATHIC GENERALIZED EPILEPSY, MUTATIONS THEREOF AND METHOD USING SAMETO ASSESS, DIAGNOSE, PROGNOSIS OR TREAT EPILEPSY	ROULEAU, GUY
<u>60295168</u>	Not Issued	020	06/01/2001	GENE-BASED ASSAYS FOR THERAPEUTIC AGENTS USEFUL IN TREATING NEUROLOGICAL DISORDERS	ROULEAU, GUY

Inventor Search Completed: Search Completed: No Records to Display.

	Last Name	First Name
Search Another:	<input type="text" value="ROULEAU"/>	<input type="text" value="GUY"/>
Inventor	<input type="button" value="Search"/>	

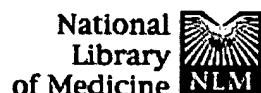
(To go back use Back button on your browser toolbar.)

Back to [PALM](#) | [ASSIGNMENT](#) | [OASIS](#) | Home page

L Number	Hits	Search Text	DB	Time stamp
1	940	(polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly\$ adj1 binding adj1 protein)	USPAT; EPO; DERWENT	2002/02/26 10:28
2	945	(polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly\$2 adj1 binding adj1 protein)	USPAT; EPO; DERWENT	2002/02/26 10:35
3	898	(polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly? adj1 binding adj1 protein)	USPAT; EPO; DERWENT	2002/02/26 10:29
4	2	((polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly? adj1 binding adj1 protein)) WITH (repeat or GCG or CpG)	USPAT; EPO; DERWENT	2002/02/26 10:30
5	4	((polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly? adj1 binding adj1 protein)) same (repeat or GCG or CpG)	USPAT; EPO; DERWENT	2002/02/26 10:30
6	30	((polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly? adj1 binding adj1 protein)).clm.	USPAT; EPO; DERWENT	2002/02/26 10:33
7	151	Rouleau.in. or brais.in.	USPAT; EPO; DERWENT	2002/02/26 10:33
8	3	Rouleau.in. and brais.in.	USPAT; EPO; DERWENT	2002/02/26 10:34
9	2	((polyA adj1 binding adj1 protein) or PAB or PABII or (PAB adj1 II) or (poly\$2 adj1 binding adj1 protein)) and (Rouleau.in. or brais.in.)	USPAT; EPO; DERWENT	2002/02/26 10:37

(FILE 'HOME' ENTERED AT 11:09:18 ON 26 FEB 2002)

FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:09:30 ON 26 FEB 2002
L1 1058 S (PAB OR PABI OR PAB2) (L) (REPEAT OR SEQUENCE OR HUMAN)
E POLYA
L2 198 S E3 (L) (BINDING (L) PROTEIN)
L3 9 S L2 AND (PAB OR PAB2 OR PABI)
L4 3786 S L2 OR (PAB OR PAB2 OR PABI)
L5 57 S L4 (L) (REPEAT OR CPG)
L6 517 S L4 (L) (REPEAT OR CPG OR MUTATION OR ALTERATION)
L7 200 DUPLICATE REMOVE L6 (317 DUPLICATES REMOVED)
L8 140 S L7 AND HUMAN
L9 3 S L8 AND CPG



PubMed Nucleotide Protein Genome Structure PopSet Taxonomy OMIM Book

Search PubMed

Limits

Preview/Index

History

Clipboard

Details

Entrez PubMed

1: Genomics 1998 Sep 1;52(2):201-4



Restriction map of a YAC and cosmid contig encompassing the oculopharyngeal muscular dystrophy candidate region on chromosome 14q11.2-q13.

Xie YG, Rochefort D, Brais B, Howard H, Han FY, Gou LP, Maciel P, The BT, Larsson C, Rouleau GA.

Center for Research in Neuroscience, McGill University, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec, H3G 1A4, Canada.

Related Resources

As part of our effort to clone positionally the oculopharyngeal muscular dystrophy (OPMD) gene, we constructed a YAC contig, a cosmid contig, and an EcoRI restriction map of the OPMD candidate region. The YAC contig spans more than 2 Mb and encompasses the loci D14S283 and D14S990 and the cardiac alpha and beta myosin heavy chain genes (MYH6 and MYH7). A 700-kb cosmid contig containing the D14S990 and the myosin genes and a long-range restriction map covering the region between D14S990 and the MYH6 and MYH7 gene cluster were established. A detailed EcoRI restriction map of the cosmid contig was determined, and five putative CpG islands were identified. Based on these data, the four loci were mapped within an approximately 600-kb region with the following centromere to telomere order: D14S283, D14S990, MYH6, and MYH7. The YAC and cosmid contigs will facilitate the identification of genes lying within the OPMD candidate interval.

Copyright 1998 Academic Press.

PMID: 9782086 [PubMed - indexed for MEDLINE]

[Write to the Help Desk](#)

[NCBI](#) | [NLM](#) | [NIH](#)

[Department of Health & Human Services](#)

[Freedom of Information Act](#) | [Disclaimer](#)

SHORT COMMUNICATION

Restriction Map of a YAC and Cosmid Contig Encompassing the Oculopharyngeal Muscular Dystrophy Candidate Region on Chromosome 14q11.2-q13

Ya-Gang Xie, Daniel Rochefort, Bernard Brais, Heidi Howard, Fei-Yu Han, Lu-Ping Gou, Patricia Maciel, Bin Tean The,* Catherina Larsson,* and Guy A. Rouleau¹

Center for Research in Neuroscience, McGill University, and Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada; and *Department of Molecular Medicine, Clinical Genetics Unit, Karolinska Hospital, L-6 Building, S-171 76 Stockholm, Sweden

Received December 2, 1997; accepted May 22, 1998

As part of our effort to clone positionally the oculopharyngeal muscular dystrophy (OPMD) gene, we constructed a YAC contig, a cosmid contig, and an *Eco*RI restriction map of the OPMD candidate region. The YAC contig spans more than 2 Mb and encompasses the loci D14S283 and D14S990 and the cardiac α and β myosin heavy chain genes (MYH6 and MYH7). A 700-kb cosmid contig containing the D14S990 and the myosin genes and a long-range restriction map covering the region between D14S990 and the MYH6 and MYH7 gene cluster were established. A detailed *Eco*RI restriction map of the cosmid contig was determined, and five putative CpG islands were identified. Based on these data, the four loci were mapped within an approximately 600-kb region with the following centromere to telomere order: D14S283, D14S990, MYH6, and MYH7. The YAC and cosmid contigs will facilitate the identification of genes lying within the OPMD candidate interval. © 1998 Academic Press

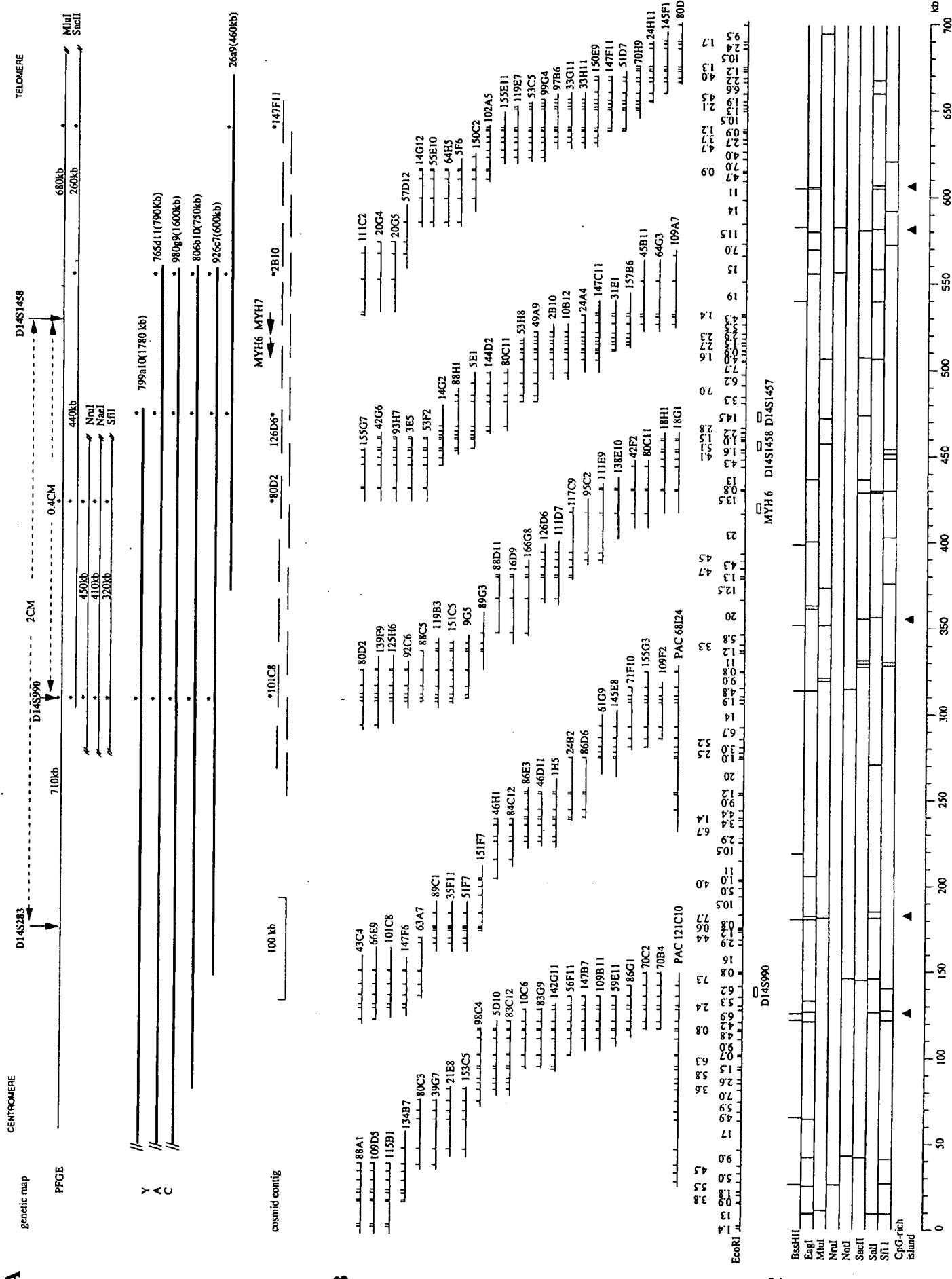
Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant disease characterized by late onset (usually after the age of 50) progressive drooping of eyelids (ptosis) and difficulty swallowing (dysphagia) (11). Based on a linkage study of French Canadian families with OPMD, we have previously mapped the OPMD locus to a 3.6-cM interval between marker D14S50 and two intronic (CA)_n markers from the cardiac β myosin heavy chain gene (D14S1457 and D14S1458) on human chromosome 14q11.2-q13 (3). This interval has been further reduced to 2 cM between D14S283 and two cardiac β heavy chain gene markers (4). To characterize the OPMD candidate region, determine the chromosomal orientation of MYH6 and MYH7, and identify genes in this region, we have es-

¹ To whom correspondence should be addressed at Department of Neurology, Montreal General Hospital, L7-224, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada. Telephone: (514) 937-6011, ext. 4235. Fax: (514) 934-8265. E-mail: mi32@musica.mcgill.ca.

tablished a physical map containing the loci D14S283, D14S990, MYH6, and MYH7, consisting of a 2-Mb YAC contig and a cosmid contig with an *Eco*RI restriction map that covers a total of 700 kb.

Probes for D14S283 (124–152 bp) and D14S990 (125–153 bp) were generated by PCR amplification using published primer sequences (5). Probes E35M6 (253 bp) and E4M7 (254 bp) are the PCR products of exon 35 of MYH6 and exon 4 of MYH7, respectively (6, 8), amplified using intronic primers E36M6-A (5' TGGAGAAAGGCTATGAA-ATCAGGT3') and E36M6-B (5' CCCAAGGCCTGTT-CTGTCTTA3'); E4M7-A (5' TTGAGGAAGGAGGGAGC3') and E4M7-B (5' CATGGATGGAGCAAGAACAG-AGAT3'). Primers for D14S990 and D14S283 (S990-A and S283-A), E35M6-A, and E4M7-A (described above) and intronic primers for exon 1 of MYH6 (E1M6-A: 5' GGGGAAA-CGGGATATAAGGAAC3'), exon 39 of MYH6 (E39M6-B: 5' GCCCCCTACTGCCCTGAT3'), exon 1 of MYH7 (E1M7-A: 5' GTGACAACAGCCCTTCTAAATCC3'), and exon 40 of MYH7 (E40M7-B: 5' ATTGCTTTATTCT-GCTTCCTC3') were used as oligonucleotide probes.

D14S283, D14S990, E4M7, and E36M6 were used as start points in the construction of the genomic contigs. YAC 26a9 was identified by PCR screening of a human genomic YAC library (1) with markers E35M6 and E4M7, and YACs 806b10 and 926c7 were identified for the D14S990 locus. Three YACs containing locus D14S283 were selected from the Genome Data Base (GDB). All YAC clones were obtained from the Canadian Genetic Diseases Network (CGDN) DNA Core Facility. The six YACs were characterized by Southern analysis of PFGE-separated YAC blots using *Eco*RI fragments from cosmids containing D14S283, D14S990, MYH6, and MYH7. The sizes of YACs were estimated to be 460 (26A9), 600 (926c7), 750 (806b10), and 790 kb (765d11). The sizes of YACs 799a10 (1780 kb) and 980g9 (1600 kb) were obtained from the GDB. YAC 26a9 was confirmed to contain both MYH6 and MYH7, and YACs 806b10, 765d11, and 980g9 contain the MYH6 and MYH7



gene cluster, D14S990 and D14S283. Only D14S990 and D14S283 detected YACs 799a10. These results allowed us to contig all the YACs, except YAC 26a9, and map loci D14S283 and D14S990 to a 600-kb region.

In parallel, the Los Alamos gridded chromosome 14-specific cosmid library, constructed from flow-sorted chromosomes cloned into vector scos-1 and consisting of approximately 16,000 recombinants, was used to isolate 17 cosmids using the MYH6, MYH7, E35M6, and E4M7 probes. The cosmid library was screened by direct hybridization to 14 gridded filters, each containing 1152 clones, constructed within the laboratory and processed as described in Lafrenière *et al.* (9). Based on the occurrence of same-sized *Eco*RI fragments, these cosmids were assembled into a contig spanning 96 kb. Hybridizing E35M6 and E4M7 mapped MYH6 and MYH7 back to the contig to *Eco*RI Southern blots of the cosmids. Using a similar strategy, we identified and characterized three cosmids corresponding to loci D14S283 and 12 cosmids for D14S990.

Simultaneously, *Alu*-PCR amplified products from YAC 26a9 were used to probe the cosmid library. Nineteen cosmids were identified, some of which had already been assigned to the cosmid contig containing the MYH genes. The cosmids that did not map to the previously identified contigs were used to probe the cosmid library. This resulted in expansion of the contig containing MYH genes in both directions and construction of several independent short contigs ranging in size from 60 to 80 kb.

Cosmid contigs were constructed by bidirectional walking from the MYH6 and MYH7 gene cluster, D14S283 and D14S990, as described in Lafrenière *et al.* (9). As chromosome walking progressed, we encountered a low "clonal represented region." Single-copy *Eco*RI fragments from cosmid 153C5 (1.2 kb) and cosmid 155G3 (2.0 kb) were used to screen a total human PAC library (RPCI-1; information on the library is available at <http://bacpac.med.buffalo.edu>; Ref. 7). PAC 68I24 and PAC 121C10 were identified. PAC 68I24 helped us to anchor the region containing cosmid 71F10 and cosmid 86D6, resulting in all the cosmids becoming part of a large contig. The contig is composed of 110 cosmids starting from

D14S990 and the MYH6 and MYH7 genes and spans 700 kb (Fig. 1). The PAC clones were obtained from the CGDN DNA Core Facility.

The *Eco*RI restriction map of the contig was constructed by identifying shared restriction fragments in overlapping clones, as described in Lafrenière *et al.* (9). It yields an estimated span of 700 kb centered between the D14S990 locus and the MYH6 and MYH7 genes (Fig. 1B). Based on the previously reported genetic maps placing D14S283 centromeric to D14S990 and MYH (5), and the orientation of the cosmid contig within the YAC contig, we established that MYH6 is centromeric to MYH7 (Fig. 1). The MYH6 and MYH7 genes were placed on our *Eco*RI restriction map using oligo probes from both ends of the two genes (E1M6-A, E39M6-B, E1M7-A, E40M7-B) (Fig. 1A).

To characterize further the OPMD candidate region, we performed PFGE mapping, as described in Rutledge *et al.* (10), with three DNA markers chosen from the cosmid contig. These *Eco*RI fragments were isolated from near the MYH6 and MYH7 genes (80D2 and 147F11) or from the cosmids containing locus D14S990 (101C8). A 4.8-kb *Eco*RI fragment from 80D2, a 2-kb *Eco*RI fragment from 147F11, and a 5.3-kb *Eco*RI fragment from the D14S990 cosmid (101C8) were used to probe several PFGE Southern filters individually. Results show that cosmids 80D2 and D14S990 cohybridize to a 710-kb *Mlu*I fragment, a 410-kb *Nae*I fragment, a 450-kb *Nru*I fragment, a 440-*Sac*II fragment, and a 320-*Sfi*I fragment. The probe from cosmid 147F11 identified only a 680-kb *Mlu*I and a 260-kb *Sac*II fragment, but failed to recognize any bands from DNA digested with other enzymes. These results confirmed the YAC contig, the chromosomal orientation of the cosmid contig, and the chromosomal orientation of MYH6 and MYH7 (Fig. 1A).

Based on the definition of a CpG-rich island as a clustering of four or more of the following eight restriction enzymes, *Bss*HII, *Eag*I, *Mlu*I, *Nru*I, *Not*I, *Sac*II, *Sal*I, and *Sfi*I, within a 2-kb interval, we could identify five separate CpG-rich islands dispersed throughout the contig (Fig. 1C; Refs. 2, 9).

We report a detailed physical map of the OPMD candidate region, which includes a YAC contig and a cosmid contig, as well as both a long-range and an

FIG. 1. YAC and cosmid contig of the OPMD candidate region on 14q11.2-q13. (A) A genomic contig with a long-range restriction map: the approximately 2-Mb YAC contig consists of six overlapping YAC clones, depicted by long horizontal boldface lines. The names and approximate sizes of the YACs are shown on the right. The location of the cosmid contig is shown. Each cosmid is indicated by a short horizontal line that represents approximately 40 kb. The contig spans approximately 700 kb. The arrows represent the location, genomic size, and transcriptional orientation of the MYH7 and MYH6 genes. The centromere is to the left, and the telomere is to the right. The sizes and location of *Mlu*I, *Nae*I, *Nru*I, *Sac*II, and *Sfi*I restriction fragments are shown above the YAC contig. The cosmids used as probes to characterize the YAC contig and PFGE mapping are indicated by an asterisk shown below them. A summary of genetic mapping results for markers D14S283, D14S990, and D14S1458 is also shown at the top. The genetic distances from locus D14S1458 to D14S990 and D14S283 are given. (B) Details of cosmid and PAC contigs with *Eco*RI restriction map. Relative overlaps of 110 cosmids and two PACs that include MYH6, MYH7 (D14S1457 and D14S1458), and locus D14S990 are shown; the locations of these loci are shown as rectangles beneath the restriction map. Overlaps are based on sharing of common-size *Eco*RI fragments (vertical lines in each clone). Clones are designated by their coordinates in the gridded library. Consensus *Eco*RI restriction map of the contig is based on the cosmid overlaps. Numbers above the maps correspond to the sizes of *Eco*RI fragments in kb. (C) Restriction map of *Bss*HII, *Eag*I, *Mlu*I, *Nru*I, *Not*I, *Sac*II, *Sal*I, and *Sfi*I relative to the *Eco*RI map. Putative CpG islands are indicated as dark arrowheads.

*Eco*RI restriction map. The YAC contig is composed of six overlapping YACs, spans a distance of more than 2 Mb, and contains loci D14S283, D14S990, MYH6, and MYH7. The cosmid contig within this region spans approximately 700 kb. A long range PFGE restriction map covers the region between D14S990 and the MYH6 and MYH7 gene cluster, and an *Eco*RI restriction map has been established for the entire cosmid contig. We have mapped D14S283, D14S990, MYH6, and MYH7 to an approximately 600-kb region and determined the order and the chromosomal orientation of these markers (from centromere to telomere—D14S283, D14S990, MYH6, and MYH7).

We have found that establishing a restriction map simultaneously with the construction of a cosmid contig facilitates chromosome walking. This practice helps identify the most extreme end-cosmid, confirms the overlaps, and helps exclude the possibility of false-positive links caused by cross-hybridization or rearranged clones.

Our physical map and genomic contig will also help to elucidate this subchromosomal region, to map and characterize known genes, and to help identify novel genes in this region. The cosmid contig will also facilitate the sequencing of chromosome 14.

ACKNOWLEDGMENTS

This work was supported by the Muscular Dystrophy Association (USA), the Association Française contre les Myopathies, and the Jewish Foundation of Greater Philadelphia. G.A.R. is supported by the Medical Research Council of Canada and the Fonds de Recherche en Santé du Québec.

REFERENCES

- Albertsen, H. M., Abderrahim, H., Cann, H. M., Dausset, J., Le Paslier, D., and Cohen, D. (1990). Construction and characterisation of a yeast artificial chromosome library containing seven
- Bird, A. P. (1986). CpG-rich islands and the function of DNA methylation. *Nature* **321**: 209–213.
- Brais, B., Xie, Y.-G., Sanson, M., Morgan, K., Weissenbach, J., Korczyn, A. D., Blumen, S. C., Fardeau, M., Tomé, F. M. S., Bouchard, J. P., et al. (1995). The oculopharyngeal muscular dystrophy locus maps to the region of the cardiac alpha and beta myosin heavy chain genes on chromosome 14q11.2–q13. *Hum. Mol. Genet.* **4**: 429–434.
- Brais, B., Bouchard, J. P., Gosselin, F., Xie, Y.-G., Fardeau, M., Tomé, F. M. S., and Rouleau, G. A. (1997). Using the full power of linkage analysis in 11 French Canadian families to fine map the oculopharyngeal muscular dystrophy gene. *Neuromusc. Dis.* **7**: S70–S74.
- Dib, C., Faure, S., Fizames, C., Samson, D., Drouot, N., Vignal, A., Millasseau, P., Marc, S., Hazan, J., Seboun, E., Lathrop, M., Gyapay, G., Morissette, J., and Weissenbach, J. (1996). A comprehensive genetic map of the human genome based on 5,264 microsatellites. *Nature* **380**: 152–154.
- Epp, T. A., Dixon, I. M., Wang, H. Y., Sole, M. J., and Liew, C. C. (1993). Structural organization of the human cardiac α -myosin heavy chain gene (MYH6). *Genomics* **18**: 505–509.
- Ioannou, P., Amemiya, C., Garnes, J., Kroisel, P., Shizuya, H., Chen, C., Batzer, M., and de Jong, P. (1994). A new bacteriophage P1-derived vector for the propagation of large human DNA fragments. *Nat. Genet.* **6**: 84–89.
- Jaenicke, T., Diederich, K. W., Haas, W., Schleich, J., Lichter, P., Pfordt, M., Bach, A., and Vosberg, H. P. (1990). The complete sequence of the human beta-myosin heavy chain gene and a comparative analysis of its product. *Genomics* **8**: 194–206.
- Lafrenière, R. G., de Jong, P. J., and Rouleau, G. A. (1995). A 405-kb cosmid contig and *Hind*III restriction of the progressive myoclonus epilepsy type I (EPMI) candidate region in 21q22.3. *Genomics* **29**: 288–290.
- Ruttledge, M. H., Xie, Y.-G., Han, F.-Y., Giovannini, M., Janson, M., Fransson, I., Werelius, B., Delattre, O., Thomas, G., Evans, G., and Dumanski, J. P. (1994). Physical mapping of the NF2/meningioma region on human chromosome 22q12. *Genomics* **19**: 52–59.
- Victor, M., Hayes, R., and Adams, R. D. (1962). Oculopharyngeal muscular dystrophy: Familial disease of late life characterised by dysphagia and progressive ptosis of the eye lids. *N. Engl. J. Med.* **267**: 1267–1272.